

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

EPSTEIN *et al.*

Patent No. 6,767,741

Issued: July 27, 2004

For: **Metal Binding Compounds And
Their Use In Cell Culture Medium
Compositions**

Confirmation No.: 8261

Atty. Docket: 0942.4630001/RWE/BJD
(IVGN 214)

**Request for Certificate of Correction Under
37 C.F.R. § 1.322 for Office Mistake**

Attn: Certificate of Correction Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

It is hereby requested that a Request for Certificate of Correction under 37 C.F.R. § 1.322 be issued for the above captioned U.S. Patent. This Certificate of Correction is being requested due to mistakes which appear in the claims of the printed patent. Applicants believe the mistakes were incurred through the fault of the Patent and Trademark Office. Therefore, Applicants believe no fee is due with this request. However, if a fee is due, please charge Deposit Account 50-3994.

Specifically, the printed patent contains the following errors for which a Certificate of Correction is respectfully requested:

In the claims

On January 9, 2004, Applicants filed an amendment of the claims. (Exhibit A.) Thereafter, an Examiner's amendment (Exhibit B) of the claims, dated March 11, 2004, was

entered which amended, *inter alia*, claims 8, 12, 54, 31 and 45 which correspond to claims 1, 6, 13, 15, and 20, respectively, of the captioned U.S. patent. Claims 1, 6, 13, 15, and 20 of the above captioned U.S. patent (Exhibit C) are not consistent with the Examiner's amendment. Therefore, Applicants request the following corrections:

Claim 1, line 11, "3-hydroxypyrid-2-one" should read --3-hydroxypyrid-2-one, 1-hydroxypyrid-2-one--.

Claim 6, line 1, "3" should read --1--.

Claim 13, line 2, "1xmedium" should read --1X medium--.

Claim 15, line 12, "1-hydroxypyrid-2-one 1-methyl-3-hydroxypyrid-2-one," should read --1-hydroxypyrid-2-one, 1-methyl-3-hydroxypyrid-2-one,--.

Claim 20, line 3, "vanadium" should read --vanadium--.

Remarks

The above-noted corrections are made only to correct typographical errors. Applicants believe these corrections do not involve such changes in the patent as would constitute new matter or would require reexamination.

A completed Form PTO/SB44 accompanies this request, with the above-noted corrections printed thereon. Accordingly, a Certificate of Correction is believed proper and issuance thereof is respectfully requested.

Respectfully submitted,

/Douglas A. Golightly/
Douglas A. Golightly
Agent for Applicants
Registration No. 51,244
240-379-4686

Date: November 17, 2006

Exhibit A

- 3 -

EPSTEIN *et al.*
Appl. No.09/650,339

Listing of the Claims

This listing of claims will replace all prior versions, and listings of claims in the application.

1. (Currently amended) A serum free cell culture medium comprising at least one transition metal binding compound or at least one transition element complex, said complex comprising at least one transition element or a salt or ion thereof complexed to at least one transition metal-binding compound, wherein said medium is capable of supporting the cultivation of a cell *in vitro*, wherein said transition metal binding compound is selected from the group consisting of a polyol, 2-hydroxypyridine-N-oxide, 1,3,5-N,N',N''-tris(2,3-dihydroxybenzoyl)aminomethylbenzene, ethylenediamine-N,N'-tetramethylenephosphonic acid, trisuccin, an acidic saccharide, a glycosaminoglycan, diethylenetriaminepentaacetic acid, nitrilotriacetic acid, mono-substituted 2,2'-bipyridine, bis-substituted 2,2'-bipyridine, tris-substituted 2,2'-bipyridine, a hydroxamate derivative, an amino acid derivative, deferoxamine, ferrioxamine, iron basic porphine, porphyrin and derivatives thereof, DOTA-lysine, a texaphyrin, a sapphyrin, a polyaminocarboxylic acid, an α -hydroxycarboxylic acid, a polyethylenecarbamate, picolinic acid, 4-pyridoxic acid, 3-hydroxy-2-pyridinemaltol, maltol, ethyl maltol, Ustilago ferrichrome, nicotinic acid-N-oxide, 2-hydroxy-nicotinic acid and IRC011.

2. (Previously presented) The medium of claim 1, wherein said transition element is selected from the group consisting of scandium, titanium, vanadium, chromium, manganese, iron, cobalt, nickel, copper, zinc, yttrium, zirconium, niobium, molybdenum,

technetium, rubidium, rhodium, palladium, silver, cadmium, lanthanum, hafnium, tantalum, tungsten, rhenium, osmium, iridium, platinum, gold, mercury, actinium, and salts thereof.

3. (Original) The medium of claim 1, wherein said transition element is iron, or a salt or ion of iron.

4. (Cancelled)

5. (Original) The medium of claim 1, wherein said metal-binding compound is a polyol.

6. (Original) The medium of claim 5, wherein said polyol is sorbitol or fructose.

7. (Original) The medium of claim 5, wherein said polyol is sorbitol.

8. (Currently amended) A serum free cell culture medium comprising at least one transition metal binding compound or at least one transition element complex, said complex comprising at least one transition element or a salt or ion thereof complexed to at least one transition metal-binding compound, wherein said medium is capable of supporting the cultivation of a cell *in vitro*, wherein said transition metal-binding compound is a hydroxypyridine derivative selected from the group consisting of 2-hydroxypyridine-N-oxide, 3-hydroxy-4-pyrone, 3-hydroxypyrid-2-one, 3-hydroxypyrid-2-one, ~~3-hydroxypyrid-4-one~~,

1-hydroxypyrid-2-one, ~~1,2-dimethyl-3-hydroxypyrid-4-one~~, 1-methyl-3-hydroxypyrid-2-one, ~~3-hydroxy-2(1H)-pyridinone~~, ~~nicotinic acid-N-oxide~~, and 2-hydroxy-nicotinic acid.

9. (Cancelled)

10. (Original) The medium of claim 8, wherein said hydroxypyridine derivative is 2-hydroxypyridine-N-oxide.

11. (Original) The medium of claim 3, wherein said transition element ion is a ferrous ion or a ferric ion.

12. (Original) The medium of claim 3, wherein said salt of said transition element salt is FeCl_3 .

13. (Original) The medium of claim 1, wherein said transition element complex is sorbitol- FeCl_3 .

14. (Cancelled)

15. (Previously presented) The cell culture medium of claim 1, said medium further comprising one or more ingredients selected from the group of ingredients consisting of at least one amino acid, at least one vitamin, at least one inorganic salt, at least one organic salt, at least one trace metal, at least one nucleotide, at least one buffering salt, at least one

sugar, at least one lipid and at least one hormone.

16. (Original) The cell culture medium of claim 1, wherein said cell culture medium supports the growth or cultivation of at least one cell selected from a group consisting of eukaryotic cells and prokaryotic cells.

17. (Original) The cell culture medium of claim 16, wherein said eukaryotic cells are selected from a group consisting of fish cells, plant cells, animal cells, insect cells and avian cells.

18. (Original) The cell culture medium of claim 17, wherein said cells are selected from a group consisting of 293 cells, PER-C6 cells, CHO cells, COS cells and Sp2/0 cells.

19. (Cancelled)

20. (Original) The cell culture medium of claim 1, wherein said medium is a defined medium.

21. (Previously presented) The medium of claim 20, wherein said transition element is iron, or a salt or ion thereof.

22. (Previously presented) The medium of claim 1, wherein said medium does not contain transferrin.

23. (Original) The medium of claim 1, wherein said medium does not contain animal derived metal carriers.

24. (Currently amended) A serum-free cell culture medium obtained by combining a cell culture medium with at least one transition metal binding compound or at least one transition element complex, said complex comprising at least one transition element or a salt or ion thereof complexed to at least one transition metal-binding compound, wherein said medium is capable of supporting the cultivation of a cell *in vitro*, wherein said transition metal binding compound is selected from the group consisting of a polyol, 2-hydroxypyridine-N-oxide, 1,3,5-N,N',N''-tris(2,3-dihydroxybenzoyl)aminomethylbenzene, ethylenediamine-N,N'-tetramethylenephosphonic acid, trisuccin, an acidic saccharide, a glycosaminoglycan, diethylenetriaminepentaacetic acid, nitrilotriacetic acid, mono-substituted 2,2'-bipyridine, bis-substituted 2,2'-bipyridine, tris-substituted 2,2'-bipyridine, a hydroxamate derivative, an amino acid derivative, deferoxamine, ferrioxamine, iron basic porphine, porphyrin and derivatives thereof, DOTA-lysine, a texaphyrin, a sapphyrin, a polyaminocarboxylic acid, an α -hydroxycarboxylic acid, a polyethylenecarbamate, picolinic acid, 4-pyridoxic acid, ~~3-hydroxy-2-pyridineethyl maltol~~, maltol, ethyl maltol, Ustilago ferrichrome, nicotinic acid-N-oxide, 2-hydroxy-nicotinic acid and IRC011.

25. (Previously presented) The medium obtained according to claim 24, wherein said transition element is selected from the group consisting of scandium, titanium, vanadium, chromium, manganese, iron, cobalt, nickel, copper, zinc, yttrium, zirconium,

niobium, molybdenum, technetium, rubidium, rhodium, palladium, silver, cadmium, lanthanum, hafnium, tantalum, tungsten, rhenium, osmium, iridium, platinum, gold, mercury, actinium, and salts thereof.

26. (Original) The medium obtained according to claim 24, wherein said transition element is iron, or a salt or ion thereof.

27. (Cancelled)

28. (Original) The medium obtained according to claim 24, wherein said metal-binding compound is a polyol.

29. (Original) The medium obtained according to claim 28, wherein said polyol is sorbitol, dextran, or fructose.

30. (Original) The medium obtained according to claim 29, wherein said polyol is sorbitol.

31. (Currently amended) A serum-free cell culture medium obtained by combining a cell culture medium with at least one transition metal binding compound or at least one transition element complex, said complex comprising at least one transition element or a salt or ion thereof complexed to at least one transition metal-binding compound, wherein said medium is capable of supporting the cultivation of a cell *in vitro*, wherein said metal-

binding compound is a hydroxypyridine derivative selected from the group consisting of 2-hydroxypyridine-N-oxide, 3-hydroxy-4-pyrone, 3-hydroxypyrid-2-one, ~~3-hydroxypyrid-4-one~~, 1-hydroxypyrid-2-one, ~~1,2-dimethyl-3-hydroxypyrid-4-one~~, 1-methyl-3-hydroxypyrid-2-one, ~~3-hydroxy-2(1H)-pyridinone~~, ~~nicotinic acid-N-oxide~~, and 2-hydroxy-nicotinic acid.

32. (Cancelled)

33. (Previously presented) The medium obtained according to claim 31, wherein said hydroxypyridine derivative is 2-hydroxypyridine-N-oxide.

34. (Original) The medium obtained according to claim 24, wherein said transition element ion is a ferrous ion or a ferric ion.

35. (Original) The medium obtained according to claim 34, wherein said salt of said transition element salt is FeCl_3 .

36. (Original) The medium obtained according to claim 24, wherein said transition element complex is sorbitol- FeCl_3 .

37 - 43. (Cancelled)

44. (Previously presented) A kit for the cultivation of a cell *in vitro*, said kit comprising:

- (a) at least one first container containing at least one first component selected from the group consisting of one or more cell culture media or media ingredients, and one or more cells, and
- (b) at least one second container containing at least one second component selected from the group consisting of one or more transition metal binding compounds and at least one transition element complex, said complex comprising at least one transition element or a salt or ion thereof complexed to at least one transition metal-binding compound.

45. (Previously presented) The kit of claim 44, wherein said transition element is selected from the group consisting of scandium, titanium, vanadium, chromium, manganese, iron, cobalt, nickel, copper, zinc, yttrium, zirconium, niobium, molybdenum, technetium, rubidium, rhodium, palladium, silver, cadmium, lanthanum, hafnium, tantalum, tungsten, rhenium, osmium, iridium, platinum, gold, mercury, actinium, and salts thereof.

46. (Original) The kit of claim 44, wherein said transition element is iron, or a salt or ion thereof.

47. (Currently amended) The kit of claim 44, wherein said metal-binding compound is selected from the group consisting of a polyol, a hydroxypyridine derivative, 1,3,5-N,N',N''-tris(2,3-dihydroxybenzoyl)aminomethylbenzene, ethylenediamine-N,N'-tetramethylenephosphonic acid, nitrilotriacetic acid, trisuccin, an acidic saccharide, a glycosaminoglycan, diethylenetriaminepentaacetic acid, mono-substituted 2,2'-bipyridine,

bis-substituted 2,2'-bipyridine, tris-substituted 2,2'-bipyridine, a hydroxamate derivative, an amino acid derivative, deferoxamine, ferrioxamine, iron basic porphine, porphyrin and derivatives thereof, DOTA-lysine, a texaphyrin, a sapphyrin, a polyaminocarboxylic acid, an α -hydroxycarboxylic acid, a polyethylenecarbamate, picolinic acid, 4-pyridoxic acid, 3-hydroxy-2-pyridineethyl maltol, maltol, ethyl maltol, Ustilago ferrichrome, nicotinic acid-N-oxide, 2-hydroxy-nicotinic acid and IRC011.

48. (Original) A composition comprising the culture medium of claim 1 and at least one cell.

49. (Original) The composition of claim 48, wherein said cell is selected from the group consisting of a plant cell, a mammalian cell, a bird cell, an insect cell, or a fish cell.

50. (Original) The composition of claim 49, wherein said mammalian cell is a human cell.

51. (Original) The composition of claim 48, wherein said cell is a normal cell.

52. (Original) The composition of claim 48, wherein said cell is an abnormal cell.

53. (Original) The composition of claim 52, wherein said abnormal cell is a transformed cell, an established cell, or a cell derived from a diseased tissue sample.

54. (Original) The medium of claim 1, wherein said medium is a 1X medium formulation.

55. (Original) The medium of claim 1, wherein said medium is a concentrated medium formulation.

56. (Original) The medium of claim 1, wherein said transition metal binding compound is ferrous gluconate.

57. (Original) The medium of claim 1, wherein said transition metal binding compound is acetohydroxamic acid.

58. (Original) The medium obtained according to claim 24, wherein said transition metal binding compound is ferrous gluconate.

59. (Original) The medium obtained according to claim 24, wherein said transition metal binding compound is acetohydroxamic acid.

60 - 61. (Cancelled)

Exhibit B

Application/Control Number: 09/650,339

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Art Unit: 1651

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with F. Cottingham on 3/3/04.

The application has been amended as follows:

IN THE CLAIMS

Claims 1, 5-7, 13, 16, 17, 24-26, 28-30, 36, 47-53, 56-59 have been canceled.

Claim 2, line 1, "1" has been changed to ---8---.

Claim 3, line 1, "1" has been changed to ---8---.

Claim 8, line 1, after "serum free" has been inserted ---mammalian---.

Claim 8, line 5, after "cultivation of a" has been inserted --mammalian--.

Claim 8, line 7, the second compound, "3-hydroxypyrid-2-one" has been deleted.

Claim 11, line 1, "3" has been changed to ---8---.

Claim 12, line 1, "3" has been changed to ---8---.

Claim 15, line 1, "1" has been changed to ---8---.

Claim 18, line 1, "17" has been changed to ---8---.

Claim 20, line 1, "1" has been changed to ---8---.

Claim 22, line 1, "1" has been changed to ---8---.

Claim 23, line 1, "1" has been changed to ---8---.

Claim 31, line 1, after "serum-free", has been inserted --mammalian--.

Art Unit: 1651

Claim 31, line 5, after "cultivation of a" has been inserted ---mammalian---.

Claim 34, line 1, "24" has been changed to ---31---.

Claim 44, line 4, after "one or more" has been inserted ---mammalian---.

Claim 44, last line, has been inserted

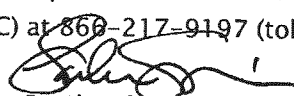
---wherein said transition metal-binding compound is a hydroxypyridine derivative selected from the group consisting of 2-hydroxypyridine-N-oxide, 3-hydroxy-4-pyrone, 3-hydroxypyrid-2-one, 1-hydroxypyrid-2-one, 1-methyl-3-hydroxypyrid-2-one and 2-hydroxy-nicotinic acid---.

Claim 54, line 1, "1" has been changed to ---8---.

Claim 55, line 1, "1" has been changed to ---8---.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Saucier whose telephone number is (571) 272-0922. The examiner can normally be reached on Monday, Tuesday, Wednesday.

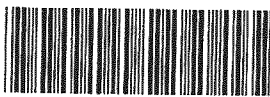
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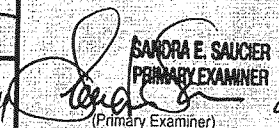
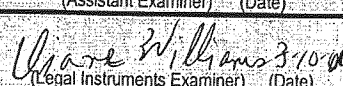


Sandra Saucier

Primary Examiner

Art Unit 1651

Issue Classification 	Application No.	Applicant(s)	
	09/650,339	EPSTEIN ET AL.	
	Examiner	Art Unit	
	Sandra Saucier	1651	

ISSUE CLASSIFICATION									
ORIGINAL				CROSS REFERENCE(S)					
CLASS	SUBCLASS			CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)				
435	404			435	405				
INTERNATIONAL CLASSIFICATION									
C12N	5100								
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			/						
(Assistant Examiner) (Date)				 SANDRA E. SAUCIER PRIMARY EXAMINER (Primary Examiner)			Total Claims Allowed: 21		
 (Legal Instruments Examiner) (Date)							O.G. Print Claim(s) 1		

<input type="checkbox"/> Claims renumbered in the same order as presented by applicant				<input type="checkbox"/> CPA				<input type="checkbox"/> T.D.				<input type="checkbox"/> R.1.47			
Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original		
	1	15	31		61		91		121		151		181		
2	2		32		62		92		122		152		182		
3	3	16	33		63		93		123		153		183		
	4	17	34		64		94		124		154		184		
	5	18	35		65		95		125		155		185		
	6		36		66		96		126		156		186		
	7		37		67		97		127		157		187		
1	8		38		68		98		128		158		188		
	9		39		69		99		129		159		189		
4	10		40		70		100		130		160		190		
5	11		41		71		101		131		161		191		
6	12		42		72		102		132		162		192		
	13		43		73		103		133		163		193		
	14	19	44		74		104		134		164		194		
7	15	20	45		75		105		135		165		195		
	16	21	46		76		106		136		166		196		
	17		47		77		107		137		167		197		
8	18		48		78		108		138		168		198		
	19		49		79		109		139		169		199		
9	20		50		80		110		140		170		200		
10	21		51		81		111		141		171		201		
11	22		52		82		112		142		172		202		
12	23		53		83		113		143		173		203		
	24	13	54		84		114		144		174		204		
	25	14	55		85		115		145		175		205		
	26		56		86		116		146		176		206		
	27		57		87		117		147		177		207		
	28		58		88		118		148		178		208		
	29		59		89		119		149		179		209		
	30		60		90		120		150		180		210		

metal binding compounds, failed to support the growth of the cells over three passages.

The ability of various metal binding compounds to substitute for transferrin in the culture of Sp2/0 cells was determined and the results are seen in Table 3. When added to the medium formulation un-complexed, the metal binding compound is listed alone, when added as a complex with a transition metal, the source of the transition metal is listed with the metal binding compound.

TABLE 3

EFFECT OF METAL BINDING COMPOUNDS ON THE GROWTH OF Sp2/0 CELLS			
Metal binding compound tested	Conc.		
	25 μ M	50 μ M	100 μ M
2-Hydroxypyridine-N-Oxide	98	93	89
3-Hydroxypyridine-N-Oxide · Ferric Chloride	55	54	57
Sorbitol · Ferric Chloride	94	55	60
Deferoxamine Mesylate · Ferric Chloride	0	0	0
(All lines tested at 5, 10, 20 μ M)	(5 μ M)	(10 μ M)	(20 μ M)
Acetohydroxamic Acid · Ferric Chloride	40	48	47
(Sp2 tested at 5, 10, 20 μ M)			
Serine Hydroxamate · Ferric Chloride	46	66	62
Glycine · Ferric Chloride	34	61	56
Nitriloacetic Acid · Ferric Chloride	88	87	70
Nitriloacetic Acid	0	0	0
3-Hydroxy-2-Methyl-4-Pyrone (Maltol)	0	0	0
3-Hydroxy-2-Methyl-4-Pyrone · Ferric Chloride	60	71	75
2-Ethyl-3-Hydroxy-4-Pyrone (Ethyl Maltol)	0	75	116
Diethylenetriamine Penta-Acetic Acid · Ferrous Sulfate	54	90	91
2-Hydroxynicotinic Acid · Ferric Chloride	64	82	85
Ferrous Gluconate · Ascorbic Acid Phosphate	92	94	93
Glutamine · Ferric Chloride	36	55	65
Asparagine · Ferric Chloride	36	51	54
Cysteine · Ferrous Sulfate	85?	79	67
4-Pyridoxic Acid · Ferric Chloride	40	73	76
2-Pyridinecarboxylic Acid · Ferric Chloride	0	30	48
Morpholine · Ferric Chloride	54	64	81
3-Hydroxy-2-Nitroppyridine · Ferric Chloride	52	62	72
Kojic Acid	0	0	0
Kojic Acid · Ferric Chloride	0	0	0
Ferrous Sulfate	91	103	94
Ferric Chloride	55	73	74

Having now fully described the present invention in some detail by way of illustration and example for purposes of clarity of understanding, it will be obvious to one of ordinary skill in the art that the same can be performed by modifying or changing the invention within a wide and equivalent range of conditions, formulations and other parameters without affecting the scope of the invention or any specific embodiment thereof, and that such modifications or changes are intended to be encompassed within the scope of the appended claims.

All publications, patents and patent applications mentioned in this specification are indicative of the level of skill of those skilled in the art to which this invention pertains, and are herein incorporated by reference to the same extent as if each individual publication, patent or patent application was specifically and individually indicated to be incorporated by reference.

What is claimed is:

1. A serum free mammalian cell culture medium comprising at least one transition metal binding compound or at least one transition element complex, said complex comprising at least one transition element or a salt or ion thereof

complexed to at least one transition metal-binding compound, wherein said medium is capable of supporting the cultivation of a mammalian cell in vitro, wherein said transition metal-binding compound is a hydroxypyridine derivative selected from the group consisting of 2-hydroxypyridine-N-oxide, 3-hydroxy-4-pyrone, 3-hydroxypyrid-2-one, 1-methyl-3-hydroxypyrid-2-one, and 2-hydroxy-nicotinic acid.

2. The medium of claim 1, wherein said transition element is selected from the group consisting of scandium, titanium, vanadium, chromium, manganese, iron, cobalt, nickel, copper, zinc, yttrium, zirconium, niobium, molybdenum, technetium, rubidium, rhodium, palladium, silver, cadmium, lanthanum, hafnium, tantalum, tungsten, rhenium, osmium, iridium, platinum, gold, mercury, actinium, and salts thereof.

3. The medium of claim 1, wherein said transition element is iron, or a salt or ion of iron.

4. The medium of claim 1, wherein said hydroxypyridine derivative is 2-hydroxypyridine-N-oxide.

5. The medium of claim 1, wherein said transition element ion is a ferrous ion or a ferric ion.

6. The medium of claim 3, wherein said salt of said transition element salt is FeCl_3 .

7. The cell culture medium of claim 1, said medium further comprising one or more ingredients selected from the group of ingredients consisting of at least one amino acid, at least one vitamin, at least one inorganic salt, at least one organic salt, at least one trace metal, at least one nucleotide, at least one buffering salt, at least one sugar, at least one lipid and at least one hormone.

8. The cell culture medium of claim 1, wherein said cells are selected from a group consisting of 293 cells, PER-C6 cells, CHO cells, COS cells and Sp2/0 cells.

9. The cell culture medium of claim 1, wherein said medium is a defined medium.

10. The medium of claim 9, wherein said transition element is iron, or a salt or ion thereof.

11. The medium of claim 1, wherein said medium does not contain transferrin.

12. The medium of claim 1, wherein said medium does not contain animal derived metal carriers.

13. The medium of claim 1, wherein said medium is a 1 \times medium formulation.

14. The medium of claim 1, wherein said medium is a concentrated medium formulation.

15. A serum-free mammalian cell culture medium obtained by combining a cell culture medium with at least one transition metal binding compound or at least one transition element complex, said complex comprising at least one transition element or a salt or ion thereof complexed to at least one transition metal-binding compound, wherein said medium is capable of supporting the cultivation of a mammalian cell in vitro, wherein said metal-binding compound is a hydroxypyridine derivative selected from the group consisting of 2-hydroxypyridine-N-oxide, 3-hydroxy-4-pyrone, 3-hydroxypyrid-2-one, 1-hydroxypyrid-2-one 1-methyl-3-hydroxypyrid-2-one, and 2-hydroxy-nicotinic acid.

16. The medium obtained according to claim 15, wherein said hydroxypyridine derivative is 2-hydroxypyridine-N-oxide.

17. The medium obtained according to claim 15, wherein said transition element ion is a ferrous ion or a ferric ion.

18. The medium obtained according to claim 17, wherein said salt of said transition element salt is FeCl_3 .

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19. A kit for the cultivation of a cell in vitro, said kit comprising:

- (a) at least one first container containing at least one first component selected from the group consisting of one or more mammalian cell culture media or media ingredients, and one or more cells, and
- (b) at least one second container containing at least one second component selected from the group consisting of one or more transition metal binding compounds and at least one transition element complex, said complex comprising at least one transition element or a salt or ion thereof complexed to at least one transition metal-binding compound wherein said transition metal-binding compound is a hydroxypyridine derivative selected from the group consisting of

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2-hydroxypyridine-N-oxide, 3-hydroxy-4-pyrone, 3-hydroxypyrid-2-one, 1-hydroxypyrid-2-one, 1-methyl-3-hydroxypyrid-2-one and 2-hydroxynicotinic acid.

20. The kit of claim 19, wherein said transition element is selected from the group consisting of scandium, titanium, vanadium, chromium, manganese, iron, cobalt, nickel, copper, zinc, yttrium, zirconium, niobium, molybdenum, technetium, rubidium, rhodium, palladium, silver, cadmium, lanthanum, hafnium, tantalum, tungsten, rhenium, osmium, iridium, platinum, gold, mercury, actinium, and salts thereof.

21. The kit of claim 19, wherein said transition element is iron, or a salt or ion thereof.

* * * * *

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CERTIFICATE OF CORRECTION**Page 1 of 1

PATENT NO. : 6,767,741

APPLICATION NO.: 09/650,339

ISSUE DATE : July 27, 2004

INVENTOR(S) : David A. Epstein; Paul J. Battista; Dale F. Gruber; David A Judd

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Claim 1, line 11, "3-hydroxypypyrid-2-one" should read --3-hydroxypyrid-2-one, 1-hydroxypyrid-2-one--.

Claim 6, line 1, "3" should read --1--.

Claim 13, line 2, "1xmedium" should read --1X medium--.

Claim 15, line 12, "1-hydroxypyrid-2-one 1-methyl-3-hydroxypyrid-2-one," should read
--1-hydroxypyrid-2-one, 1-methyl-3-hydroxypyrid-2-one,--.

Claim 20, line 3, "van adium" should read --vanadium--.

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